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HARVARD MEDICAL SCHOOL
DEPARTMENT OF DERMATOLOGY

THOMAS B. FITZPATRICK, M.D., Ph.D.
Professor of Dermatology, Emeritus

Dermatology Service
Massachusetts General Hospital
Boston, Massachusetts 02114
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July 2, 1992

William E. Gilbertson, Pharm. D.
Director, Monograph Review Division
Office of OTC Drugs
Food and Drug Administration, 4FN-210
7520 Standish Place
Rockville, MD 20855

Dear Dr. Gilbertson:

On May 20th, we participated in a meeting at the FDA to review the safety of 2% hydroquinone as a skin depigmenting agent.

During that presentation we reviewed our experiences with hydroquinone, and now wish to summarize our remarks so that they can be included in the record.

Of the several depigmenting agents (over 20) that have been studied in our laboratory, as well as by other investigators, hydroquinone is the only skin hypopigmenting agent that is both safe and effective at, and somewhat above, the (2%) OTC concentration. At concentrations above 3%, hydroquinone is irritant. Serious side effects may occur only at high concentrations exceeding 4 to 5% HQ when used continuously for a long period of time. For treatment of melasma and other pigmentary problems, we recommend 2% HQ in combination with retinoic acid and topical sunscreens (SPF 30). Two percent HQ is also recommended in maintenance therapy of melasma. Unlike the depigmentation induced by monobenzyl-ether of hydroquinone, the hypopigmentation induced by HQ is not permanent; in fact, the bleached skin can be repigmented. It is this property which makes HQ a better bleaching agent. A potent skin bleaching agent is 4-isopropyl catechol, but it causes skin sensitization. Hydroquinone does not cause any skin sensitization or allergic reaction. Hydroquinone formulations must be well stabilized against oxidation.

Hydroquinone at 2% concentration is a non-irritant, non-sensitizing agent that exerts mild hypopigmenting effects in brown or black skin, provided the individual avoids exposure to sunlight and uses opaque sunscreens (SPF $\geq$15-30).

There is no evidence that this compound promotes skin cancer, with or without sunlight. Furthermore, in our clinical research experience of over 35 years, ochronosis reportedly associated with hydroquinone use is a very rare event in the U.S. and one which should not affect the OTC safety of 2% hydroquinone. Ochronosis cases that have been reported in literature resulted from unsupervised use of hydroquinone formulations that invariably contained HQ greater than 5 to 7%.

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In summary, it is our opinion that 2% hydroquinone, as a skin hypopigmenting agent for epicutaneous application, is a useful OTC drug. In dermatology, there is no other safe and effective OTC drug for achieving uniform and predictive hypopigmenting action on skin.

Please include this letter in the record of your rulemaking on OTC hydroquinone.

Sincerely yours,

Thomas B. Fitzpatrick, M.D., Ph.D.
Professor of Dermatology, Emeritus

Madhu A. Pathak, M.B., Ph.D.
Senior Associate in Dermatology
(Research Professor)

/ea

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE:

FROM: Director
Monograph Review Staff (HFD-810)

SUBJECT: Material for Docket No. 78N-0065

TO: Dockets Management Branch (HFA-305)

☑ The attached material should be placed on public display under the above referenced Docket No.

☐ This material should be cross-referenced to Comment(s) No. _____.

W E. Gilbertson

William E. Gilbertson, Pharm. D.

Attachment

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AUG 3 1992

Thomas B. Fitzpatrick, M.D., Ph.D
Professor of Dermatology, Emeritus
Department of Dermatology
Harvard Medical School
Massachusetts General Hospital
Boston, MA 02114

Dear Dr. Fitzpatrick:

I am responding to your letter of July 2, 1992, summarizing your presentation during the hydroquinone feedback meeting held on May 20, 1992, between the Nonprescription Drug Manufacturers Association's Hydroquinone Task Group and FDA. You stated that 2% hydroquinone, as a skin hypopigmenting agent for epicutaneous application, is a useful OTC drug, and there is no other safe and effective OTC drug for achieving uniform and predictive hypopigmenting action on the skin. Further, you stated that there is no evidence that hydroquinone promotes skin cancer, and in 35 years of clinical research experience, ochronosis reportedly associated with hydroquinone use is a very rare event in the United States and should not effect the OTC safety of this ingredient. You requested that your letter be included in the record for the rulemaking on OTC skin bleaching drug products.

The FDA is currently reviewing all available scientific data on the safety and effectiveness of hydroquinone, including data presented by you and other members of the dermatological community during the May 20, 1992 feedback meeting regarding hydroquinone's medicinal importance and clinical benefit as an OTC drug. The agency appreciates the summary of your experiences with OTC skin bleaching drug products containing 2% hydroquinone and is including your letter in the administrative record for the agency's current rulemaking for OTC skin bleaching drug products.

Thank you for sharing your views with us.

Sincerely yours,

William E. Gilbertson, Pharm. D.
Director, Monograph Review Staff
Office of OTC Drug Evaluation
Center for Drug Evaluation and Research

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EXECUTIVE SECRETARIAT

HFD-800

May 19, 1992

Dr. David A. Kessler
Commissioner
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Kessler:

We understand that the Food & Drug Administration is reviewing the regulatory status of 2% Hydroguinone as the active ingredient in over-the-counter fade creams designed to treat hyperpigmentation.

We want to congratulate you for taking the initiative in studying this product. Historically, products used by women have not been subject to the appropriate scrutiny, and we do know that many older women use these products. As you proceed with the study we believe it is important that consumers input be included in its design.

We are hopeful that the findings will result in this product continuing to be available over the counter, thereby giving women continued choice in its use.

Sincerely,

Joan A. Kuriansky
Executive Director

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CDER EXECUTIVE
SECRETARIAT STAFF
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Older Women's League
666 11th Street NW, Suite 700 · Washington DC 20001 · (202)783-6686 · (202)638-2356 FAX

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